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the technology, the problems and the possibilities**

Mickey Gjerris & Gábor Vajta

SUMMARY

DANISH CENTRE FOR BIOETHICS AND RISK ASSESSMENT

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SUMMARY

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Summary of Project report 6

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Report summary

Since the birth of the cloned sheep Dolly a range of other mammalian species have been cloned using the traditional SCNT technology that was used when producing Dolly and using other methodologies. The success rates remain low (less than 5%) no matter what kind of methodology. However, the so-called Hand-made Cloning approach where the methodology enables the nuclei transfer to be performed at a lower cost (both in equipment and trained persons) seems to have some advantages, mainly that it makes cloning cheaper per produced animal.

The reasons to the low success rates have not been fully understood yet, but it seems that both methodological choices (donor cell lines, cell nutrition, maturation period of egg cell, level of technical skill etc) and other so-called epigenetic factors that are connected to the way that the cloned embryo reacts to the reprogramming and the in vitro phase are involved.

The problems associated with animal cloning show themselves from the first stages of the development of the cloned egg and until after the birth of the animals. Problems frequently occurring are:

- Placental abnormalities
- Fetal overgrowth, prolonged gestation
- Stillbirth, hypoxia, respiratory failure and circulatory problems, lack of post-natal vigour
- Increased body temperature at birth
- Malformations in the urogenital tract (hydronephrosis, testicular hypoplasia)
- Malformations in liver and brain
- Immune dysfunction, lymphoid hypoplasia, anaemia, thymic atrophy
- Bacterial and viral infections

According to some recent information, considerable success in partial or almost total elimination of these developmental problems has been achieved in several laboratories by performing slight modifications in the technique. Another positive sign is that offspring of the cloned animals do not show any increase in developmental problems compared to control animals, thus confirming the epigenetic and transient nature of the cloning-related syndromes, and also widening the possibilities of practical application.

Even so, the low success rates are the most important technical factor hampering the economic feasibility of a range of applications of farm animal cloning that can be found in the literature. These include:

- **Basic research:** Using the cloning technology to gain a deeper insight into the fertilization process and the development of the early foetus.
- **Disease models:** Used together with genetic modification cloning can produce animals that mimic human diseases and thus perhaps lead to a better understanding of these and provide tailored animals that can be used to test new drugs on.
- **Bioreactors:** Used together with genetic modification cloning can be used to produce animals that can be used as biological factories that express human proteins that can be harvested and used as medicine.
- **Agricultural applications:** Used alone or together with genetic modification cloning can perhaps be used to produce animals that will increase productivity, animal welfare or the quality of food products.
- **Pets, endangered species, etc.:** Cloning can be used for a range of more exotic purposes, e.g. cloning pet cats or cloning indi-

viduals from endangered species to increase the breeding populations.

It is debated whether the technology can actually be used for all these purposes, since not only the low success rates but also the fact that cloning does not produce genetically identical individuals and that two almost genetically identical individuals might differ strongly on the phenotypic level. This pertains especially to the agricultural applications where high success rates, public acceptance and the production of individual animals with specific desirable traits are necessary to make cloning economically feasible.

The future of animal cloning is thus not clear, It can be regarded as a technology that has a lot of theoretical applications but according to the present efficiency it must be foreseen that in the near future it will mostly play a role within basic research and biomedicine where the value of each animal is very high. Whether the technology will become interesting from an agricultural point of view remains to be seen. There is no consensus on this subject among scientists.

This report seeks to evaluate the state of the art of farm animal cloning based on a literature review with additional information gathered at a workshop held in Seville may 2005, co-organised by the Institute of Prospective Technological Studies (European Commission: DG JRC-IPTS, Sustainability in Agriculture, Food and Health unit), the Danish Centre for Bioethics and Risk Assessment (CeBRA), and the European Commission DG RTD (Bio-technology, Agriculture and Food directorate) as part of the project CLONING IN PUBLIC.